

REMARKS

Consideration of this application in view of the above amendments and following remarks is respectfully requested. This Amendment serves as the submission accompanying Applicants' Request for Continued Examination (RCE) filed pursuant to 37 C.F.R. §1.114. Claims 1-3, 6, 9, 20, 25-37, 40-45, 54, 59-69, 71, 73-75 and 79-81 are now pending. Claims 1, 20, 35, 54 and 73 have been amended. Claims 4-5, 7-8, 10-14, 16, 19, 21-22, 38-39, 46-47, 50, 53, 55-56, 70, 72, 76-78 have been canceled.

***Claim Rejections – 35 U.S.C. § 102***

Claims 1-14, 16, 19, 20, 25, 29, 31, 35, 36-47, 50, 53, 54, 59, 61, 70 and 72 stand rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, obvious under 35 U.S.C. § 103(a) over, US 5,162,430 ("Rhee").

The basis of the Examiner's rejection is set forth in the Final Office Action at pages 2-4 and is not repeated herein for the purpose of brevity. Rather, Applicants will address Item 9 of the Office Action, in which the Examiner stated that "while Rhee does not teach synthetic polylysine, the collagen-PEG having lysine groups meet the limitation of poly(alkylene oxide) having amino nucleophilic groups."

Without acquiescing to the rejections in the Office Action or prejudice to future prosecution of the previously pending claims in a related application, Applicants have amended claims 1, 35 and 73 to delete poly(alkylene oxide) having m nucleophilic groups. Amended claim 1 now recites a synthetic polylysine as the first crosslinkable component, as do amended claims 35 and 73. Because Rhee does not teach synthetic polylysine, as acknowledged by the Examiner (Item 9 of the Office Action), Applicants submit that claims 1, 35 and 74 (and their respective dependent claims) are novel over Rhee.

Further, Applicants submit that claims 1, 35 and 73 are not obvious in view of Rhee because a prima facie case of obviousness has not been established. Rhee describes conjugates of collagen crosslinked with di-functionalized polyethylene glycols. The claimed invention differs from Rhee in that a synthetic polylysine is used, instead of collagen. Collagens

are proteins with complex chemical structures (with multiple types of nucleophilic groups), configurations and degradation profiles. Synthetic polylysines are linear polypeptides with repeating units of lysine. The Office Action has not articulated a reason for one skilled in the art to modify Rhee's collagen conjugate with the claimed synthetic polylysine conjugates.

Moreover, Applicants have discovered that, unlike collagen conjugates, the claimed conjugate is less susceptible to enzymatic cleavage by matrix metalloproteinases, such as collagenase, and are therefore not readily degradable *in vivo* and, as such, are expected to have greater long-term persistence *in vivo* than prior art collagen compositions (*see*, paragraph [0024] of the subject application).

Accordingly, Rhee fails to satisfy a *prima facie* showing of obviousness (or, even if shown, is sufficiently rebutted by the above remarks), and Applicants request that this ground of rejection be withdrawn as applied to claim 1, 35 and 73 and their respective dependent claims.

#### ***Claim Rejections – 35 U.S.C. § 103***

Claims 1-14, 16, 19-22, 25-47, 50, 53-56 and 59-84 stand rejected under 35 U.S.C. § 103(a) as being obvious over Rhee in view of US 5,505,952 ("Jiang").

Amended claim 1 is directed to a method for augmenting tissue by crosslinking two crosslinkable components *in situ* or at a tissue site. This is not disclosed or suggested by Rhee, alone or in combination with Jiang. As discussed above, there is no suggestion or motivation to modify Rhee's disclosure with regard to collagen conjugate to arrive at the claimed invention. The Examiner sought to cure this deficiency by relying on Jiang's disclosure to show that polyamino acid can be used to promote tissue repair.

Applicants respectfully submit that there is no suggestion or motivation to simply substitute the collagen of Rhee with the polyamino acid of Jiang. Unlike the claimed invention or Rhee, Jiang is limited to crosslinking polyamino acid (including polylysine) with small molecules and is wholly unsuited for crosslinking *in situ*. For instances, prior to use (*e.g.*, repairing tissue), Jiang's polyamino acid was crosslinked, dried and heated in vacuum, rehydrated, ground up, freeze-dried and cast into a sheet or film before being applied to the tissue site (*see*, Example 1 of Jiang). Thus, one skilled in the art would not look to Jiang for

augmenting or repairing tissue by crosslinking two components *in situ*. Accordingly, claim 1, as amended, is not obvious in view of the combination of Rhee and Jiang.

Amended claims 35 and 73 are also not obvious in view of the combination of Rhee and Jiang, for the same reasons as set forth above.

***Conclusion***

In view of the above amendments and remarks, allowance of claims 1-3, 6, 9, 20, 25-34, 35-37, 40-45, 54, 59-69, 71, 73-75 and 79-81 is respectfully requested. A good faith effort has been made to place this application in condition for allowance. However, should any further issue require attention prior to allowance, the Examiner is requested to contact the undersigned at (206) 622-4900 to resolve the same.

Respectfully submitted,

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